Both isomers appear to interact with lipid bilayers in a similar fashion. Our results suggest that Aβ mediated disruption of ionic homeostasis may occur by a direct pathway of ion channel formation and may not need to rely on interactions with membrane receptors. Understanding the mechanism of peptide-membrane interaction and insertion at nanoscale resolution is essential for therapeutic design aiming to control and prevent Aβ pore formation. Funded by NCI Contract HHSN261200800001E (RN) and NIH (National Institute on Aging AG028709) extramural program (RL).

**2995-Pos Board B765**
**Scanning Probe Microscopy of Serpin Polymers**
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Serpins belong to a superfamily of structurally homologous proteins with metastable native structures. Their metastability is crucial in performing their function as regulators of serine and cysteine protease cascades. However, mutated variants of serpins found in patients with serpinopathies are often prone to polymerization. The most widespread serpinopathy is related to the Z variant of antitrypsin, which forms toxic polymers in the liver leading to liver degeneration. The understanding of polymerization mechanism holds the key to disease prevention, diagnostics and cures. Several models of serpin polymerization have been proposed. Still, the structure of *in vivo* formed polymers is unknown, and the relevance of *in vitro* created oligomers to disease related structures is far from established. Here we employed atomic force microscopy (AFM) to compare topography of *in vitro* and *in vivo* formed antitrypsin polymers and oligomers. We established morphometric features of Z monomers and *in vitro* formed dimers with different types of linkage. Moreover, we found a remarkable heterogeneity of unit types and their arrangement in polymer strands isolated from the Z variant mutant mouse liver. Even within the same strand there were examples of a linear arrangement of monomer units and of compact arrangement of dimers. The *in vitro* formed wild type oligomer preparations contained structures resembling the native Z variant structures from the liver. Still, the partition of types of polymers was strikingly distinct, with compact monomer arrangement and polymerized dimers frequenting the *in vitro* samples. In addition to AFM, we used scanning tunneling microscopy (STM) to study the orientation of units in polymers based on the proteins surface charge. Summarizing, SPM imaging provided the unique data on a high heterogeneity of polymers and pointed at certain types of monomer linkages that might help explain the mechanism of serpin polymerization.

## Vibrational Spectroscopy

**2996-Pos Board B766**
**Deep-Uvrr Spectroscopy Studies of Amyloidogenic Transthyretin Fragments**
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The protein transthyretin (TTR) has been implicated as the pathogen in several amyloid diseases. Normally a transport protein for thyroxine, amyloidosis occurs when the protein aggregates and deposits in organ tissue as β-sheet structured amyloid fibrils. The formation of amyloid fibril deposits associated with TTR diseases is poorly understood. In order to study amyloid fibril formation several amyloidogenic fragments of TTR have been studied in aqueous solutions. It has been suggested that the amyloidogenic fragments TTR(10-20) and TTR(105-115) contain portions of the protein essential to aggregation and amyloid fibril formation, however, neither have been studied in the presence of cell-like lipid membranes. Here, we present the first studies comparing aqueous and model membrane solution studies of TTR(10-20) and TTR(105-115) via deep-ultraviolet resonance Raman spectroscopy. Initial results suggest a change in peptide secondary structure upon interaction with lipid membranes.

**2997-Pos Board B767**
**In Vivo Molecular Labeling of Halogenated Volatile Anesthetics via Intrinsic Molecular Vibrations using Nonlinear Raman Spectroscopy**
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Halogenated volatile anesthetics are frequently used for inhaled anesthesia in clinical practice. No appropriate biological method has been available for visualizing their localization in action. Therefore, despite their frequent use, the mechanism of action of these drugs has not been fully investigated. We measured coherent anti-Stokes Raman scattering (CARS) spectra of sevoflurane and isoflurane, two of the most representative volatile anesthetics, and determined the low-frequency vibrational modes without nonresonant background disturbance. Molecular dynamics calculations predict that these modes are associated with multiple halogen atoms. Because halogen atoms rarely appear in biological compounds, the entire spectral landscape of these modes is expected to be a good marker for investigating the spatial localization of these drugs within the intracellular environment. Using live squid giant axons, we could detect the unique CARS spectra of sevoflurane for the first time in a biological setting.

**2998-Pos Board B768**
**Cell Surface Protein Detection using Surface-Enhanced Raman Scattering (SERS) Gold Nanoparticles**
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Surface enhanced Raman scattering (SERS) Au nanoparticles have been used as novel cell surface receptor labels for the identification of markers of interest in chronic lymphocytic leukemia (CLL) and lung cancer. Biocompatibility of the particles was improved using multiple coating and particle protection strategies. Each of these strategies facilitated different methods for the inclusion of Raman active reporter molecules, as well as for different types of targeting moieties. Characterization of the SERS nanoparticles was undertaken including quantification of the number of antibodies bound to the surface. Long-term stability of both the nanoparticle Raman signal intensity and monodispersity was assessed under standard storage conditions, as well as conditions suitable for in vitro biological experiment. The SERS labeling platform has been demonstrated as being compatible with traditional pathology protocols including flow cytometry, and stains such as giemsa. SERS detection using these particles has been adapted to models for both adherent and circulating malignancies, in addition to patient cell samples in the example of CLL. The narrow vibrational spectra of SERS particles used in this study greatly increase the multiplexed labeling potential over traditional fluorescence-based technologies. Preliminary multiplexed labeling of CLL has also been demonstrated.

**2999-Pos Board B769**
**Micro-Raman of Cancer Cells: Toward Label-Free Sorting of Circulating Tumor Cells from Whole Blood**
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Even in the early stages of cancer, circulating tumor cells (CTCs) can travel from a primary tumor site to other organs through the blood and lymphatic system. Detecting and isolating CTCs from the blood has great potential for early cancer detection and studies of metastasis. However, they are notoriously rare (a few CTCs per mL of blood) and difficult to distinguish from epithelial non-tumor cells and leukocytes. Attempts to analyze CTC genetic or protein changes in response to treatment have been hampered by the difficulty in isolating intact clonogenic cells. Toward the goal of developing a rapid, non-invasive tool for detecting and isolating live CTCs from the blood, we measured the Raman spectra of live, unlabeled single cells. Using principal components analysis (PCA), we can distinguish WBCs from cancer cells, and tumorigenic ovarian cancer cells (A2780, OVCAR2, CaOV3) from non-tumorigenic ovarian cancer cells (OV429). Adherent cell lines and suspended (laser trapped) cells from cancer patient fluid samples were measured. A microfluidic platform with pressure control has been implemented to transport such cells single-file through the Raman laser focus. Custom microfluidics are in development and will sort the live, unmarked cancer cells into separate reservoirs for cell culture. Each Raman spectrum requires ~1-2 minutes, so we are concurrently developing a faster, coherent anti-Stokes Raman scattering (CARS) microscope for higher throughput analysis. Rapid detection and sorting of live CTCs will give prognostic information and allow for observation of the effect of targeted cancer treatments via a minimally invasive blood test and possibly well before the availability of response data.

**3000-Pos Board B770**
**Study of Energetic Particle Induced Biological Effect through FTIR and Raman Micro-Spectroscopy**
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Energetic particles exist ubiquitously in nature and may cause varied biological effects which have been found useful applications such as radiotherapy of